tered to a 32-year-old woman with HBAg-positive fulminant hepatic failure. It was given after she had been in stage IV coma for 41 hours, and although all circulating HBAg then rapidly cleared from the peripheral circulation, she died in hepatic coma two and a half days later with signs of congestive heart failure. Massive hepatic necrosis was found at autopsy.

The administration of plasma containing hyperimmune antibody to HBAg may be helpful in clearing circulating antigen from the blood and may be a useful approach to be investigated further in the management of fulminant hepatitis.

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Hemochromatosis Presenting as Diabetic Ketoacidosis with Extreme Hyperglycemia

DERICK P. PASTERNAK, MD
Burlingame, California

DIAGNOSING HEMOCHROMATOSIS is frequently difficult because of its features mimicking other more common diseases, such as hepatic cirrhosis, diabetes mellitus or heart failure.[1] Even when these conditions coexist, and the index of suspicion should be high, there may be other features, such as chronic alcoholism, which may obscure the true cause of the patient's disease. As a consequence the diagnosis may not be established until the postmortem examination. This report describes a case illustrating these difficulties, and in which there was the further and unusual factor of diabetic ketoacidosis with extreme hyperglycemia to an extent hitherto unreported in this condition.

CASE: A 60-year-old man entered the hospital emergency room 27 November 1970 with complaint of vomiting and lethargy which had lasted for four days. During this time he had become progressively more lethargic, and had refused most nourishment prepared by his wife. No history of polyuria could be elicited, but he did consume large amounts of beer just before becoming ill. This was apparently not unusual for him. The past history included malaria contracted during World War II. The patient took no medications, had had no transfusions and drank no wine. Family history was unobtainable.

On physical examination the patient was observed to be cachectic and drowsy, but arousable. His breath had a fruity odor. The pulse rate was 106 per minute, respirations 30 per minute, blood

From the Dunham Army Hospital, Carlisle Barracks, PA.
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Reprint requests to: D. P. Pasternak, MD, 741 Linden Avenue, Burlingame, CA 94010.

pressure 80/60 mm of mercury and body temperature 35.6°C (96°F). The skin was dry; there was one spider angioma in the sternal notch, but no icterus or other pigment abnormality. General physical examination was unremarkable, except for dry mucous membranes and a large, firm and nodular liver. On neurological examination, the patient was oriented as to name and place, but not as to date; reflexes were hypoactive; there were no localizing signs or asterixis.

Admission laboratory data showed a hematocrit of 45 percent and leukocyte count of 8,600 per cu mm with a normal differential. Blood glucose concentration was 2,700 mg per decileter (dl), serum sodium 154, potassium 5.0, chlorine 106, CO_2 combining power 11 mEq per liter. Serum acetone was 4+; no dilutions were done. Blood urea nitrogen was 35 mg per dl. The prothrombin time was 15 seconds (control 12 seconds). The urine was straw colored and clear with 4+ sugar and acetone, no protein, 2 to 3 red blood cells and 5 to 8 white blood cells per high power field; there were no casts or bacteria seen. An x-ray film of the chest showed hyperinflated lungs, normal sized heart and no pulmonary infiltrate. The electrocardiogram showed occasional atrial and ventricular premature beats, low voltage and nonspecific ST segment abnormalities. Guaiac tests of the stool were negative.

Bed rest was prescribed and hypotonic saline solution was given intravenously at the rate of 1,000 ml per hour. Insulin was also administered intravenously and after two hours potassium chloride was added to the intravenous fluids. After 4 liters of fluid and 200 units of crystalline insulin the blood glucose was 1,260 mg per dl, CO_2 combining power 18 mEq per liter, serum acetone 4+, urine sugar 4+, urine acetone 2+. During the first seven hours of therapy, the patient received a total of 7,000 ml of fluids, 310 units of crystalline insulin, 200 mEq of potassium, and 540 mEq of sodium. The blood pressure then was 125/65 mm of mercury, pulse rate 100 per minute, the hematocrit 34 per cent, blood glucose 720 mg per dl, potassium 5.2 mEq per liter, CO_2 combining power 19 mEq per liter, serum acetone trace, urine sugar 4+, urine acetone 1+. The urine output was 3,200 ml in the first seven hours.

On the following morning the patient became gradually more disoriented and had hallucinations. Chlordiazepoxide was given for presumed delirium tremens. During the ensuing 24 hours under continuing insulin and fluid therapy the blood glucose gradually fell to 220 mg per dl. He coughed up greenish purulent sputum. On the third hospital day disorientation and coughs producing sputum persisted and the patient's temperature rose to 38.8°C (101.84°F). Blood, sputum and urine cultures were taken. A lumbar puncture yielded clear and colorless fluid under an opening pressure of 110 mm of water; there were no cells, sugar content was 157 mg per dl (simultaneous blood sugar 220 mg per dl) and protein 44 mg per dl; the fluid was cultured. An analysis of the urine showed a trace of protein, 2+ sugar, no acetone and 15 to 20 white blood cells. The patient was given cephaloridine, 1 gram administered intramuscularly every six hours. Despite this his condition continued to deteriorate. Cheyne-Stokes respirations and pulmonary edema developed and he died on the fourth day following admission to hospital. An x-ray film of the chest on the last day of life showed no infiltrate. All cultures were sterile.

Autopsy 12 hours after death showed no gross abnormalities of the heart; the lungs were edematous; the gastrointestinal tract was normal; the liver weighed 2,000 grams, was dark brown, finely nodular, and very firm; the spleen was minimally enlarged with pulp hyperplasia; there was an area of softening in the right kidney; the endocrine organs were grossly normal; in the brain, the tip of the left temporal lobe was absent. Microscopically examined, the liver showed cirrhosis with large amounts of brown pigment reacting with Prussian blue stain present in the portal triads, hepatic cells and sinusoids. There was no evidence of significant coronary atherosclerosis; iron was found in the myocardial fibers, as well as in the epicardial tissues and in the interventricular septum. The lungs had edema fluid in the alveoli and there was a neutrophilic exudate in the basal portion. The pancreas had large amounts of iron deposited both in the acinar tissues and in the islets of Langerhans. Iron deposits were also found in the stomach (epithelium), spleen, thyroid, adrenals (primarily the zona glomerulosa of the cortex) and kidneys (tubular epithelium). In addition, the right kidney had a focus of acute pyelonephritis and there were several areas containing sclerotic glomeruli and interstitium infiltrated with lymphocytes and plasma cells. In these areas the tubules were dilated and contained amorphous eosinophilic material. The pituitary gland had been submitted to the National Pituitary Bank and was not examined microscopically.

Comment

The post mortem examination clearly established that this patient had idiopathic hemochromatosis. The pattern of iron deposition is characteristic, and there was no history of multiple transfusions or excessive iron ingestion.[1-3] The disease usually presents as cirrhosis, or diabetes, or both[1,4] as in this patient; the appearance of diabetes of this severity is distinctly unusual, however. In a recent review of diabetes in 115 patients with hemochromatosis, Dymock et al[5] quoted no cases of ketoacidosis. Although the older literature is replete with cases of diabetic ketoacidosis in hemochromatosis, many of these reports originated in the pre-insulin era.[6,7]

The relative ease with which this patient's diabetic ketoacidosis was brought under control despite the extreme hyperglycemia is interesting in view of the intermittent reports in the literature of insulin resistance in patients with hemochromatosis.[7-9] It is by no means a constant finding, however.[5,10] Similarly, in view of the current controversy as to whether hemochromatosis "protects" against the atherosclerotic complications of diabetes[11,12] or does not,[5,13,14] it is relevant to point out that the patient under discussion had no retinopathic changes, only minimal coronary atherosclerosis, and the glomerular sclerosis noted in the kidneys was more compatible with chronic interstitial nephritis or chronic pyelonephritis than with the glomerulosclerosis associated with diabetes.[15]

The question of how this extreme of hyperglycemia was reached in the present case cannot be answered with any degree of certainty. Blood sugar in the range of 2,000 mg per dl and above has been described primarily in association with hyperosmolar nonketotic coma[16] but there have been occasional cases of ketoacidosis with extremely high blood sugar.[17-20] Most of these patients had received large amounts of glucose by vein,[18,19] or by mouth in the form of Coca-Cola syrup,[20] after what in retrospect had clearly been the onset of their diabetic ketoacidosis.

No such history could be elicited from this patient or his wife, but neither of them was a reliable enough historian under the circumstances. It seems reasonable to postulate that shortly before admission the patient did in fact ingest large amounts of carbohydrate, thereby acutely elevating his blood sugar to extreme levels because of the lack of circulating insulin in his state of already existing moderate diabetic ketoacidosis.

Summary

A 60-year-old alcoholic male patient presented in diabetic ketoacidosis with extreme hyperglycemia—2,700 mg per dl, a level previously unreported in this setting. After ketoacidosis had been adequately controlled delirium tremens and heart failure developed and the patient died. At post mortem examination, hemochromatosis was found.

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